R E M A R K S

1. Restriction Requirement

Applicant notes, with appreciation, the Examiner's comment that the "restriction requirement between SEQ ID NO: 1 and 3 is **withdrawn**."[1]

2. Status of the Application

Claims 1-18 are pending in the present application.

Claims 15-18 have been cancelled in response to a restriction requirement without prejudice to their renewal in a future application. Applicant's claim cancellation does not narrow the scope of any of the claims because cancellation of non-elected claims in not related to a statutory requirements for a patent but rather is related to the Patent Office's convenience for organizing searches. Applicant reserves the right to prosecute the cancelled (or similar) claims in another application(s).

New Claims 19-51 have been added to describe further embodiments of the invention. In particular, Claims 19-22, 28-31, and 37-40 are supported by the originally-filed Claims 19-20.[2] Further support for Claims 21, 22, 30, 31, 39, and 40 is in the Specification's teaching of the particular cell types:

> "The invention additionally provides a composition comprising a transgenic buffalo green monkey kidney cell expressing human decay accelerating factor, wherein the cell has a property selected from the group consisting of (a) increased sensitivity to one or more enterovirus compared to buffalo green monkey kidney cell line, and (b) permissiveness to echovirus selected from the group consisting of echovirus-6 and echovirus-11. In one embodiment, the composition further comprises a cell type other than the transgenic buffalo green monkey kidney cell line, and wherein the transgenic buffalo green monkey kidney cell and the cell type are in mixed-cell type culture. ... In a preferred embodiment, the cell type is selected from the group consisting of RD cells, H292 cells, A549 cells, MRC-5 cells, KB cells, and CaCo-2 cells. In a more preferred embodiment, the cell type is CaCo-2 cells."[3]

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[1] (Emphasis added) Paper No. 11, page 2, second paragraph.

[2] New Claim 19 corresponds to originally-filed Claim 15; new Claim 20 corresponds to originally-filed Claim 16.

[3] Specification, paragraph bridging pages 3 and 4.

See also, Specification, page 4 full paragraph; paragraph bridging pages 4 and 5; page 6, lines 9-12; page 7, last paragraph; paragraph bridging pages 8 and 9; and page 35, lines 2-8.

New Claims 23-27, 32-36, and 41-45 are supported by the Specification's teaching of the recited exemplary enteroviruses, such as the teaching that:

> "The terms "enterovirus" and "enteroviruses" refer to RNA viruses which are of the piconarviridae family as previosuly described [Fieldes Virology (1996), 3rd Edition, Publ: Lippincott S. Raben, Chapter 22]. Enteroviruses have sense RNA and non-enveloped virus particles. Enteroviruses include, without limitation, polioviruses, Coxsackie A viruses, Coxsackie B viruses, echoviruses, and enterovirus types 68, 69, 70 and 71. Polioviruses are exemplified, but not limited to poliovirus types 1, 2, and 3. Coxsackie A viruses include, without limitation, Coxsackie virus types A1, A2, A3, A4, A5, A6, A7, A8, A9, A10, A11, A12, A13, A14, A15, A16, A17, A18, A19, A20, A21, and A24. Coxsackie B viruses are exemplified by Coxsackie virus types B1, B2, B3, B4, B5, and B6. Echoviruses include, by way of example, echovirus types 1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 29, 30, 31, 32, 33, and 34."[4]

See also, Specification, paragraph bridging pages 5 and 6; paragraph bridging pages 2 and 3; and page 3, first full paragraph.

New Claims 46-51 are supported by the Specification's disclosure that the inventions' transgenic cells are susceptible and permissive to enteroviruses,[5] that the "[p]roduction of progeny virus may be determined by observation of a cytopathic effect,"[6] and that "The expanded enterovirus spectrum and increased susceptibility for the detection of enteroviruses, and the additional boost in sensitivity makes the invention's transgenic buffalo green monkey kidney cells a valuable tool for the rapid detection and/or isolation of enteroviruses in clinical laboratories."[7]

These amendments do not introduce new matter.

3. Rejection of The Claims

Claims 1-14 have been rejected on the following grounds:

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[4] Specification, paragraph bridging pages 13-14.

[5] Specification page 26, lines 10-29; page 27, lines 1-11.

[6] Specification page 27, lines 8-11; paragraph bridging pages 27 and 28.

[7] Specification page 14, lines 23-27.

A. Claims 1-3, 6, 7, and 11-14 were rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement;

B. Claims 1-4 and 6-14 were rejected under 35 U.S.C. §103(a) as being allegedly obvious over Scholl *et al.*, and Powell *et al.*, and

C. Claim 5 was rejected under 35 U.S.C. §103(a) for alleged obviousness over Scholl *et al.*, Powell *et al.*, Spiller *et al.*, and either the sequence alignment of SEQ ID NO:1 with GenEmbl accession no. M15799 of Medoff *et al.*, or the sequence alignment of SEQ ID NO:3 with GenEmbl accession M30142 of Caras *et al.*

Applicant believes that the present amendments and the following remarks traverse the Examiner's rejection of the claims. These remarks are presented in the same order as they appear above.

A. Claims 1-3, 6, 7, and 11-14 are enabled

Claims 1-3, 6, 7, and 11-14 were rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement.[8] Applicant respectfully disagrees.

The Examiner **admitted** that "[t]here is also a working example demonstrating the construction of BGMK-hDAF on pages 38-40."[9] However, the Examiner contended that this allegedly does not satisfy enablement because the lack of "public availability for the skilled artisan to compare whether a cell line produced by the method in example 1 would share the same characteristics with BGMK-hDAF recited in claim 1."

Applicant disagrees with the Examiner's contention because the Specification provides a detailed description of how to make BGMK-hDAF cells[10] by transfecting the **commercially available** BGMK cells (Diagnostic Hybrids, Inc., catalog # 53) with the exemplary **published** hDAF gene (GenBank Accession # M15799) that was cloned in the **commercially available** pcDNA3 (Invitrogen) using standard molecular biological techniques. Because generating the recited BGMK-hDAF cells was described in the Specification to use known and commercially available starting materials and to employ standard techniques, the claims are enabled.

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[8] Paper No. 11, page 2, last full paragraph.

[9] Paper No. 11, page 3, first paragraph.

[10] Specification, Example 1, pages 38-40.

Nonetheless, without acquiescing to the Examiner's arguments, but merely to expedite Applicant's business interests, Applicant has deposited the recited BGMK-hDAF cells under the terms of the Budapest Treaty with the American Type Culture Collection (ATCC) as attested to by the enclosed "Statement of Biological Culture Deposit." Since the Examiner stated that "deposit of BGMK-hDAF cells in a recognized deposit facility would satisfy the enablement requirements,"[11] Applicant respectfully requests withdrawal of this rejection.

B. Claims 1-4 and 6-14 are non-obvious over Scholl *et al.* and Powell *et al.*

Claims 1-4 and 6-14 were rejected under 35 U.S.C. §103(a) as being allegedly obvious over Scholl *et al.*[12] and Powell *et al.*[13,14] Applicant respectfully must traverse because a *prima facie* case of obviousness is not established. Furthermore, a *prima facie* case of obviousness, if arguably made, is rebutted by the prior art and by Applicant's data in the Specification.

A *prima facie* case of obviousness requires the Examiner to cite to a combination of references which (a) suggests or motivates one of skill in the art to combine the claim elements to yield the claimed combination, and (b) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish either one of these two requirements precludes a finding of a *prima facie* case and, without more, entitles Applicant to withdrawal of the rejection.[15] However, the Examiner has failed to establish, not one, but **both** requirements, thus entitling Applicant to withdrawal of this rejection, as discussed below.

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[11] Paper No. 11, page 3, first full paragraph.

[12] US patent 6,168,915.

[13] Powell *et al.* (1998) J. Gen. Virol. 79:1707-1713.

[14] Paper No. 11, page 4, last paragraph.

[15] MPEP §2143; *See, e.g., Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

i. The references do not provide motivation to make the claimed compositions

The threshold requirement for a *prima facie* case of obviousness is whether a person skilled in the art would be **motivated** to modify the reference to arrive at the **claimed invention**.[16] In particular,

> "the examiner must show *reasons* that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would *select* the elements from the cited prior art references for combination in the manner claimed."[17] Evidence of a suggestion, teaching, or motivation to modify prior art references "must be *clear and particular*."[18]

The Examiner argued that one of ordinary skill in the art "would have been motivated to express DAF taught by Powell *et al.*, in the buffalo green monkey cell lines of Scholl *et al.* to detect enterovirus haemagglutinizing strains that use DAF for cell surface attachment and entry."[19]

However, the examiner reads more into the references than is there. Scholl *et al.* discloses that buffalo green monkey kidney cells are susceptible to enterovirus infection. The Examiner **admitted** that "Scholl *et al.* does **not** teach increased susceptibility to enteroviruses of a cell line expressing the human decay accelerating factor."[20] To bridge this gap, the Examiner relied on Powell *et al.* Powell *et al.* discloses that wild type WOP mouse cells were inefficiently infected by echovirus 6 and echovirus 6', and that echovirus 7 did not infect these cells. In contrast, WOP cells transfected with decay accelerating factor (DAF) were efficiently infected by all three viruses. Powell *et al.* discloses that "[t]his result shows that DAF alone confers permissiveness to **mouse** cells for all three viruses..."[21]

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[16] *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988) and *In re Jones*, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992).

[17] (Emphasis added) *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998); *Robotic Vision Systems Inc. v. View Engineering Inc.*, 51 USPQ2d 1948 (Fed. Cir. 1999).

[18] (Emphasis added) *In re Dembiczak*, 175 F.3d 994, 50 USPQ2d 1614 (Fed. Cir. 1999), *citing C.R. Bard*, 157 F.3d 1340 at 1352, 48 USPQ2d at 1232.

[19] Paper No. 11, page 5, last paragraph.

[20] (Emphasis added) Paper No. 11, page 5, second paragraph.

[21] (Emphasis added) Powell *et al.*, paragraph bridging pages 1711 and 1712.

Importantly, however, Powell *et al.*'s statement was **limited** to the effect of DAF expression in "**mouse**" cells. Nothing in either Scholl *et al.* or Powell *et al.* suggests that expression of a decay accelerating factor in **buffalo green monkey cells** (which are recited in the instant invention's claims) would have the same effect as in Powell *et al.*'s mouse cells.

Indeed, Powell *et al.* **teaches away** from the invention. Under the law, a teaching away alone can defeat obviousness.[22] In particular, the following teaching by Powell *et al.* demonstrates that expression of decay accelerating factor in different cell types (such as CHO cells and RD cells) does **not** confer permissiveness of the cell to enterovirus and/or increased sensitivity of the cell to enterovirus:

> "In contrast, CHO transfection with DAF does **not** confer permissiveness to any CBV serotype regardless of prior adaptation (Bergelson *et al.*, 1997)."[23]
>
> "Moreover, binding of radio-labelled virus to RD cells is **not** inhibited by MAb 854 or by PIPLC treatment, which effectively removes DAF from the cell surface."[24]

In other words, contrary to the Examiner's assertion in support of "motivation," Powell *et al.* teaches that expression of decay accelerating factor by CHO cells and RD cells **neither** conferred permissiveness of these cells to enteroviruses, **nor** allowed binding of enteroviruses to the expressed protein. This **teaches away** from, rather than motivates towards, expressing decay accelerating factor in BGMK cells.

Powell *et al.* further **teaches away** from expressing decay accelerating factor because it discloses that enterovirus binding to cells is mediated via **unidentified receptor(s)** other than decay accelerating factor. For example, Powell *et al.* states that failure to confer permissiveness to CHO cells transfected with DAF:

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[22] *Winner International Royalty Corp. v. Wang,* 53 USPQ2d 1580, 202 F.3d 1340, 13449 (Fed. Cir. 2000), citing *Gambro Lundia AB v. Baxter Healthcare Crop.,* 110 F.3d 1573, 1579, 42 USPQ2d 1378, 1383 (Fed. Cir. 1997).

[23] (Emphasis added) Powell *et al.*, page 1708, first column, first paragraph.

[24] (Emphasis added) Powell *et al.*, page 1712, first column, last paragraph; second column, first paragraph. See also, statement "... the binding of EV6 and the EV9 and poliovirus controls was unaffected [by pretreatment of RD cells with monoclonal antibody MAb 845 that specifically binds to decay accelerating factor] ..." Powell *et al.*, page 1711, first column.

> "is consistent with the conclusion that **other factors** may be required for coxsackievirus infection via attachment to DAF."[25]

As to failure of enteroviruses to bind to RD cells that express decay accelerating factor, Powell *et al.* teaches that:

> "...the significantly increased levels of sDAF needed to block infection for some serotypes implies that they have a higher affinity for an **alternative, uncharacterized**, receptor. We believe the most likely interpretation of these data is that these viruses can indeed use **alternative** cellular receptors."[26]

Thus, one of skill in the art reading the above would not be impelled to express DAF in BGMK cells (as recited in the claims). This negates a *prima facie* case of obviousness.

ii. A Reasonable Expectation of Success In Making And Using The Recited Compositions Is Not Established

A fundamental requisite of establishing a *prima facie* case of obviousness is that there is a reasonable expectation of success in making and using the recited sequences.

> "[T]he reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure."[27]

The Examiner argued that one of skill in the art "would have had a reasonable expectation of success for producing the claimed invention because both Scholl *et al.* and Powell *et al.* use cells expressing recombinant genes to detect the presence of viruses...[and] because Scholl *et al.* teach that buffalo green monkey cells are susceptible to enterovirus infection and Powell *et al.* teach that cells expressing DAF are permissive to infection by hemagglutinizing enterovirus strains."[28]

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[25] (Emphasis added) Powell *et al.*, page 1708, first column, first paragraph.

[26] (Emphasis added) Powell *et al.*, page 1712, first column, last paragraph; second column, first paragraph. See also, statement "... the binding of EV6 and the EV9 and poliovirus controls was unaffected [by pretreatment of RD cells with monoclonal antibody MAb 845 that specifically binds to decay accelerating factor] ..." Powell *et al.*, page 1711, first column.

[27] *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) as cited in *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

[28] Paper No. 11, paragraph bridging pages 5 and 6.

However, this argument ignores Scholl *et al.*'s **silence** and Powell *et al.*'s **teaching away** from a reasonable expectation of success. As discussed above, Powell *et al.* teaches **failure** to bring about either binding of enterovirus to a cell expressing DAF, or permissiveness of such a cell to enteroviruses.

Furthermore, Powell *et al.*'s teaching away from a "reasonable expectation of success" is confirmed by Applicant's surprising results. Under the law, a *prima facie* case of obviousness can be rebutted by the Specification's disclosure that the claimed invention yields unexpected results.[29] In this regard, the Specification states that:

> "The properties and advantages of the invention's transgenic BGMk cells were **surprising** in view of contrary data disclosed herein when using transgenic H292 cells. In particular, data disclosed herein demonstrates that, whereas transfection of BGMK cells with vectors that express human decay accelerating factor increased both the sensitivity and permissiveness of BGMK cells to enteroviruses, in contrast, **no** increase in sensitivity to enteroviruses was observed when the same vectors were used to transfect H292 cells."[30]

Indeed, Applicant's results that are disclosed in the Specification using both laboratory isolates[31] and clinical samples[32] demonstrate:

> "...that transfection of additional copies of the hDAF gene into the H292 cells which express hDAF did **not increase or decrease** the cells' sensitivity for the detection of laboratory strains of enteroviruses. These results are in direct contrast to those obtained with BGMK-hDAF cells shown in Example 2 *supra*."[33] "In other words, transfection of additional copies of the hDAF gene into H292 cells had **no effect** on the sensitivity of detection of enteroviruses from in clinical specimens by these cells."[34]

Since the inventors' results were "**surprising**" in the face of Scholl *et al.*'s and Powell *et al.*'s disclosure, this element of a *prima facie* case of obviousness is absent.

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[29] *In re Davies,* 475 F.2d 667, 670, 177 USPQ 381, 384 (CCPA 1973).

[30] (Emphasis added) Specification, page 6, lines 11-17.

[31] Example 5 beginning on page 50 of the Specification.

[32] Example 6 beginning on page 54 of the Specification.

[33] (Emphasis added) Specification, page 54, liens 6-9.

[34] (Emphasis added) Specification, page 55, lines 1-4.

Moreover, the prior art rebuts any alleged reasonable expectation of success by demonstrating that expression of a virus receptor by a cell is **not** sufficient for binding of the virus to the cell and/or for permissiveness of the cell to the virus. For example, Harrington *et al.*[35] (copy enclosed with the supplemental IDS) teaches that:

> "Expression of the human immunodeficiency virus type 1 (HIV-1) receptor CD4 on many nonhuman and some human cell lines is **not sufficient** to permit HIV-1 infection ... [On the other hand,] CD4-expressing U373-MG (U373-CD4) cells fused to HeLa cells [that] allow HIV-entry."[36] "... **none** of the strains infected U373-CD4 cells or their $CD4^-$ parents (Table 1). On the other hand, HeLa-CD4 cells were highly permissive for the lymphocyte-tropic strain (LAI) and the primary isolate... It is noteworthy that the added expression of CD4 did **not** enhance HIV-1 production in U373-MG cells."[37]

Similarly, Chesebro *et al.*[38] (copy enclosed with the supplemental IDS) teaches that:

> "With several HIV strains in clones of human cervical carcinoma HeLa cells expressing different levels of CD4, HIV titer increased with increasing CD4 expression, In contrast, in squamous cell carcinoma cells (SCL1) and astroglial cells (U87MG), even high levels of CD4 expression **failed** to augment HIV infection."[39]

Thus, the above demonstrates that it is **unpredictable** whether or not expression of a virus receptor (such as the recited DAF) by a cell (such as the claimed invention's BGMK cells) would result in virus binding and/or cell permissiveness of that **particular cell/receptor combination**.

Because, not one, but **two** elements of a *prima facie* case of obviousness are lacking, a *prima facie* case of obviousness cannot be established. It is therefore respectfully requested that the rejection of the claims under 35 U.S.C. §103(a) be withdrawn.

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[35] Harrington *et al.* (1993) J. Virology 67(10):5939-5947.

[36] (Emphasis added) Harrington *et al.*, Abstract.

[37] (Emphasis added) Harrington *et al.*, page 5941, column 2.

[38] Chesebro *et al.* (1990) J. Virology 64(1):215-221.

[39] (Emphasis added) Chesebro *et al.*, Abstract.

C. Claim 5 is non-obvious over Scholl *et al.*, Powell *et al.*, Spiller *et al.*, GenEmbl accession no. M15799, and GenEmbl accession M30142

Claim 5 was rejected under 35 U.S.C. §103(a) for alleged obviousness over Scholl *et al.*, Powell *et al.*, Spiller *et al.*[40], and either the sequence alignment of SEQ ID NO:1 with GenEmbl accession no. M15799 of Medoff *et al.*,[41] or the sequence alignment of SEQ ID NO:3 with GenEmbl accession M30142 of Caras *et al.*[42,43] Applicant respectfully must disagree.

With respect to the alleged "motivation" to combine the references, the additionally cited Spiller *et al.* and sequence alignments do **not** overcome the above-discussed deficiencies of the primary Scholl *et al.* reference and secondary Powell *et al.* reference, namely (a) Powell *et al.*'s success was **limited to the mouse** WOP cells that were transfected with decay accelerating factor (DAF), (b) Powell *et al.* **teaches away** from the invention by teaching that CHO cells and RD cells that express decay accelerating factor do not bind to, nor are permissive for, enteroviruses, and (c) Powell *et al.* **teaches away** from the invention by teaching that enterovirus binding to cells, and the cells' permissiveness for enteroviruses is **not necessarily** mediated by binding of the enterovirus to decay accelerating factor, but is rather mediated via **alternative unidentified receptor(s)**. Thus, motivation to combine the references to arrive at the claimed compositions is lacking.

Referring to the alleged "reasonable expectation of success" in arriving at the claimed combination, the additionally cited Spiller *et al.* and sequence alignments do **not** bridge the gaps in the disclosure of Scholl *et al.* and Powell *et al.* references. These gaps are summarized as follows: (a) Scholl *et al.*'s **silence** and Powell *et al.*'s reported **failure** in two cell types (*i.e.*, CHO cells and RD cells) to bring about either binding of enterovirus to a cell expressing DAF, or permissiveness of such a cell to enteroviruses, (b) Applicant's data showing that transfection of H292 cells with hDAF do **not** show increased sensitivity to

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[40] Spiller *et al.* (2000) J. Infectious Diseases 181:340-343.

[41] Medoff *et al.* (1987) PNAS 84(7):2007-2011.

[42] Caras *et al.* (1987) Nature 325-(6104):545-549.

[43] Paper No. 11, page 6, first full paragraph.

enteroviruses, and (c) Harrington *et al.* and Chesebro *et al.* that demonstrate that expression of a virus receptor by a cell is **not** sufficient for binding of the virus to the cell and/or for permissiveness of the cell to the virus.

Because, not just one, but two elements of a *prima facie* case of obviousness are not established, a *prima facie* case of obviousness cannot stand. Applicant therefore respectfully requests withdrawal of the rejection of the claims under 35 U.S.C. §103(a).

4. New Claims 19-51 are in condition for allowance

Each of the newly added claims should be allowed since it recites compositions of independent Claims 1, 2, and 4, that are in condition of allowance for the reasons discussed above. Under *In re Ochiai*[44] and *In re Brouwer*,[45] claims which recite patentable starting materials or end products are themselves patentable.[46] For example, new Claims 19-27 and 46-47 are method claims that recite the cells of Claim 1. Also, new Claims 28-36 and 48-49 are method claims that recite the cells of Claim 2. Furthermore, new Claims 37-45 and 50-51 are method claims that recite the cells of Claim 4. Thus, new Claims 19-51 should be allowed.

CONCLUSION

All grounds of rejection and objection of the Office Action of April 21, 2003 having been addressed, reconsideration of the application is respectfully requested. Applicant

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[44] In re Ochiai, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995).

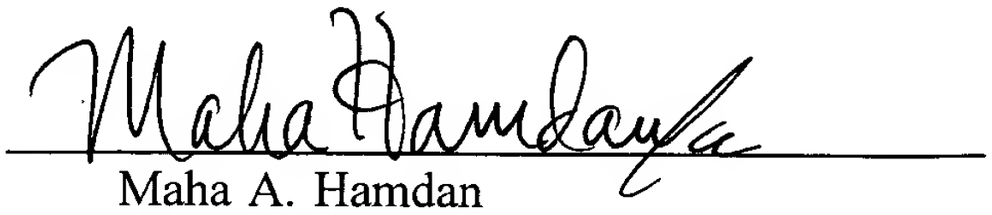
[45] *In re Brouwer*, 77 F.3d, 422, 37 USPQ2d 1663 (Fed. Cir. 1996).

[46] See also MPEP 2116.01.

respectfully requests the Examiner to **call the undersigned before drafting another written communication**, if any.

Signed on behalf of:

Dated: July 11, 2003



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APPENDIX I
AMENDMENTS TO THE CLAIMS

The following is a complete listing of all claims in the application. Status is in parenthetical expression, strike-through shows deleted matter, and underlining shows added matter.

1. (Currently Amended) A transgenic cell line designated BGMK-hDAF deposited as ATCC accession number PTA-4594.

2. (Original) A cell line established from a transgenic cell line designated BGMK-hDAF, wherein said established cell line has a property selected from the group consisting of (a) increased sensitivity to one or more enteroviruses compared to buffalo green monkey kidney cell line, and (b) permissiveness to echovirus selected from the group consisting of echovirus-6 and echovirus-11.

3. (Original) The cell line of Claim 2, wherein said cell line has the sensitivity to enterovirus of the cell line designated BGMK-hDAF.

B' cont'd

4. (Original) A transgenic buffalo green monkey kidney cell line expressing human decay accelerating factor, wherein said cell line has a property selected from the group consisting of (a) increased sensitivity to one or more enteroviruses compared to buffalo green monkey kidney cell line, and (b) permissiveness to echovirus selected from the group consisting of echovirus-6 and echovirus-11.

5. (Original) The cell line of Claim 4, wherein said human decay accelerating factor is encoded by a sequence selected from SEQ ID NO:1 and SEQ ID NO:3.

6. (Original) The cell line of Claim 4, wherein said transgenic buffalo green monkey kidney cell line has the sensitivity to enterovirus of the cell line designated as BGMK-hDAF.

7. (Original) The cell line of Claim 4, wherein said cell line is BGMK-hDAF.

8. (Original) A composition comprising a transgenic buffalo green monkey kidney cell expressing human decay accelerating factor, wherein said cell has a property selected from the group consisting of (a) increased sensitivity to one or more enterovirus compared to buffalo green monkey kidney cell line, and (b) permissiveness to echovirus selected from the group consisting of echovirus-6 and echovirus-11.

9. (Original) The composition of Claim 8, wherein said composition further comprises a cell type other than said transgenic buffalo green monkey kidney cell line, and wherein said transgenic buffalo green monkey kidney cell and said cell type are in mixed-cell type culture.

10. (Original) The composition of Claim 9, wherein said cell type is selected from the group consisting of RD cells, H292 cells, A549 cells, MRC-5 cells, KB cells, and CaCo-2 cells.

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11. (Original) A composition comprising a transgenic cell designated BGMK-hDAF.

12. (Original) The composition of Claim 11, wherein said composition further comprises a cell type other than said BGMK-hDAF cell, and wherein said BGMK-hDAF cell and said cell type are in mixed-cell type culture.

13. (Original) A composition comprising a cell established from a transgenic cell line designated BGMK-hDAF, wherein said established cell has a property selected from the group consisting of (a) increased sensitivity to one or more enteroviruses compared to buffalo green monkey kidney cell line, and (b) permissiveness to echovirus selected from the group consisting of echovirus-6 and echovirus-11.

14. (Original) The composition of Claim 13, wherein said composition further comprises a cell type other than said established cell, and wherein said established cell and said cell type are in mixed-cell type culture.

Claims 15-18 (Cancelled).

19. (New) A method for detection of one or more enterovirus in a sample, comprising:

a) providing:

i) a sample; and

ii) a composition comprising the transgenic cell line of Claim 1;

b) inoculating said cell with said sample to produce an inoculated cell; and

c) observing said inoculated cell for the presence of said one or more enterovirus.

20. (New) The method of Claim 19, wherein said composition further comprises a cell type other than said BGMK-hDAF cell, and wherein said BGMK-hDAF cell and said cell type are in mixed-cell type culture.

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21. (New) The method of Claim 20, wherein said cell type is chosen from one or more of RD cells, H292 cells, A549 cells, MRC-5 cells, KB cells, and CaCo-2 cells.

22. (New) The method of Claim 20, wherein said cell type is CaCo-2 cells.

23. (New) The method of Claim 19, wherein said enterovirus is a poliovirus.

24. (New) The method of Claim 19, wherein said enterovirus is a Coxsackie A virus.

25. (New) The method of Claim 19, wherein said enterovirus is a Coxsackie B virus.

26. (New) The method of Claim 19, wherein said enterovirus is an echovirus.

27. (New) The method of Claim 19, wherein said enterovirus is chosen from one or more of enterovirus type 68, enterovirus type 69, enterovirus type 70, and enterovirus type 71.

28. (New) A method for detection of one or more enterovirus in a sample, comprising:

a) providing:

i) a sample; and

ii) a composition comprising the transgenic cell line of Claim 2;

b) inoculating said cell with said sample to produce an inoculated cell; and

c) observing said inoculated cell for the presence of said one or more enterovirus.

29. (New) The method of Claim 28, wherein said composition further comprises a cell type other than said BGMK-hDAF cell, and wherein said BGMK-hDAF cell and said cell type are in mixed-cell type culture.

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30. (New) The method of Claim 29, wherein said cell type is chosen from one or more of RD cells, H292 cells, A549 cells, MRC-5 cells, KB cells, and CaCo-2 cells.

31. (New) The method of Claim 29, wherein said cell type is CaCo-2 cells.

32. (New) The method of Claim 28, wherein said enterovirus is a poliovirus.

33. (New) The method of Claim 28, wherein said enterovirus is a Coxsackie A virus.

34. (New) The method of Claim 28, wherein said enterovirus is a Coxsackie B virus.

35. (New) The method of Claim 28, wherein said enterovirus is an echovirus.

36. (New) The method of Claim 28, wherein said enterovirus is chosen from one or more of enterovirus type 68, enterovirus type 69, enterovirus type 70, and enterovirus type 71.

37. (New) A method for detection of one or more enterovirus in a sample, comprising:

a) providing:

i) a sample; and

ii) a composition comprising the transgenic cell line of Claim 4;

b) inoculating said cell with said sample to produce an inoculated cell; and

c) observing said inoculated cell for the presence of said one or more enterovirus.

38. (New) The method of Claim 37, wherein said composition further comprises a cell type other than said BGMK-hDAF cell, and wherein said BGMK-hDAF cell and said cell type are in mixed-cell type culture.

39. (New) The method of Claim 38, wherein said cell type is chosen from one or more of RD cells, H292 cells, A549 cells, MRC-5 cells, KB cells, and CaCo-2 cells.

40. (New) The method of Claim 38, wherein said cell type is CaCo-2 cells.

41. (New) The method of Claim 37, wherein said enterovirus is a poliovirus.

42. (New) The method of Claim 37, wherein said enterovirus is a Coxsackie A virus.

43. (New) The method of Claim 37, wherein said enterovirus is a Coxsackie B virus.

44. (New) The method of Claim 37, wherein said enterovirus is an echovirus.

45. (New) The method of Claim 37, wherein said enterovirus is chosen from one or more of enterovirus type 68, enterovirus type 69, enterovirus type 70, and enterovirus type 71.

46. (New) A method for producing one or more enterovirus, comprising:

a) providing:

i) a sample containing one or more said enterovirus, and

ii) a composition comprising the transgenic cell line of Claim 1; and

b) inoculating said transgenic cell line with said sample to produce an inoculated cell line that produces one or more said enterovirus.

47. (New) The method of Claim 46, further comprising step c) isolating the produced one or more enterovirus.

48. (New) A method for producing one or more enterovirus, comprising:

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a) providing:

i) a sample containing one or more said enterovirus, and

ii) a composition comprising the transgenic cell line of Claim 2; and

b) inoculating said transgenic cell line with said sample to produce an inoculated cell line that produces one or more said enterovirus.

49. (New) The method of Claim 48, further comprising step c) isolating the produced one or more enterovirus.

50. (New) A method for producing one or more enterovirus, comprising:

a) providing:

i) a sample containing one or more said enterovirus, and

ii) a composition comprising the transgenic cell line of Claim 4; and

b) inoculating said transgenic cell line with said sample to produce an inoculated cell line that produces one or more said enterovirus.

51. (New) The method of Claim 50, further comprising step c) isolating the produced one or more enterovirus.

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